Application No.: 10

10/566,898

Filing Date:

October 26, 2006

AMENDMENTS TO THE CLAIMS

1. (Original) A method for preparing a conjugate vaccine, the method comprising:

reacting a polysaccharide with an oxidizing agent, whereby a solution of an aldehyde-activated polysaccharide is obtained;

reacting a protein with hydrazine dichloride at an acidic pH, whereby a solution of a hydrazine-activated protein is obtained;

reacting the aldehyde-activated polysaccharide with the hydrazine-activated protein at a pH of from about 5 to about 7 in the presence of sodium cyanoborohydride, whereby a conjugate is obtained; and

neutralizing unreacted aldehyde groups with adipic acid dihydrazide, whereby a conjugate vaccine capable of stimulating an immune response is obtained.

- 2. (Original) The method according to claim 1, wherein the oxidizing agent comprises NaIO₄.
- 3. (Original) The method according to claim 1, wherein the solution of the aldehyde-activated polysaccharide is buffer exchanged with a HEPES buffer.
- 4. (Original) The method according to claim 1, wherein the solution of the aldehyde-activated polysaccharide is buffer exchanged to a pH of from about 7 to about 8
- 5. (Original) The method according to claim 1, wherein the solution of the hydrazine-activated protein is buffer exchanged with a Na₂CO₃ buffer.
- 6. (Original) The method according to claim 1, wherein the solution of the hydrazine-activated protein is buffer exchanged to a pH of from about 10.0 to about 11.0.
- 7. (Original) The method according to claim 6, wherein a pH of the solution of the hydrazine-activated protein is raised to from about 7.0 to about 11 before the solution of the hydrazine-activated protein is buffer exchanged to a pH of from about 10.0 to about 11.0.
- 8. (Original) The method according to claim 1, wherein the aldehyde-activated polysaccharide is reacted with the hydrazine-activated protein at a ratio of from about 1:1.6 to about 1:5.

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9. (Original) The method according to claim 1, further comprising the step of diafiltrating the conjugate vaccine, whereby substantially all unreacted compounds and unconjugated polysaccharides are removed, yielding a purified conjugate vaccine.

- 10. (Original) The method according to claim 9, further comprising the step of concentrating the purified conjugate vaccine by tangential flow ultrafiltration, yielding a concentrated purified conjugate vaccine.
- 11. (Original) The method according to claim 10, further comprising the step of adding saccharose as a stabilizer to the concentrated purified conjugate vaccine, yielding a stabilized conjugate vaccine.
- 12. (Original) The method according to claim 10, further comprising the step of freeze drying the concentrated purified conjugate vaccine, yielding a dried conjugate vaccine.
- 13. (Original) The method according to claim 1, wherein the polysaccharide is selected from the group consisting of Meningococcal polysaccharides, Pneumococcus polysaccharides, Hemophilus influenzae type b polysaccharide, Vi polysaccharide of Salmonnella typhi, and group B Streptococcus polysaccharides.
- 14. (Original) The method according to claim 1, wherein the protein is selected from the group consisting of tetanus toxoid, diptheria toxoid, CRM₁₉₇, and meningococcal protein.